PCT/EP2003/009354

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P144902PC-La	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP2003/009354	International filing date (*day/month/year*) 22 August 2003 (22.08.2003)	Priority date (*day/month/year*) 23 August 2002 (23.08.2002)
International Patent Classification (IPC) or national classification and IPC G01N 33/569		
Applicant DEUTSCHES RHEUMA-FORSCHUNGSZENTRUM BERLIN		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 22 March 2004 (22.03.2004)	Date of completion of this report 01 October 2004 (01.10.2004)
Name and mailing address of the IPEA/EP Facsimile No.	Authorized officer Telephone No.

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International application No.
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I. Basis of the report

1. With regard to the elements of the international application:*

☐ the international application as originally filed

☒ the description:

pages 1-27, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☒ the claims:

pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages 1-14, filed with the letter of 12 August 2004 (12.08.2004)

☒ the drawings:

pages 1/3-3/3, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 11,12

because:

☒ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international preliminary examination *(specify)*:

See supplemental sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

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Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III.1

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. As concerns the second part ("and are used for cellular therapy"), claims 11 and 12 relate to subject matter which, in the opinion of this Authority, is covered by PCT Rule 67.1(iv). Therefore no opinion on the industrial applicability of these claims will be established (PCT Article 34(4)(a)(i)).

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V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-10	YES
	Claims	11-14	NO
Inventive step (IS)	Claims	1-10	YES
	Claims	11-14	NO
Industrial applicability (IA)	Claims	1-10, 13, 14	YES
	Claims		NO

2. Citations and explanations

2. The following documents are taken into consideration:

D1: WO99/58977
D2: BERNER B ET AL, ANNALS OF THE RHEUMATIC DISEASES, Vol. 59, 2000, pages 190-195
D3: SCHOENBECK U ET AL: INT. J. BIOCHEM. CELL BIOL., Vol. 32, No. 7, July 2000, pages 687-693
D4: VALMORI D ET AL: CANCER RES., Vol. 59, No. 9, 1999, pages 2167-2173

3. Closest prior art for claims 1 to 10:
D1 discloses a method of concentrating "effector cells" as a precursor population for selecting activated T cells. Positive selection by means of CD154 ("CD40L")-specific antibodies is mentioned *inter alia* (see D1, page 26, lines 8 to 20, and page 27, lines 19 to 24). An effector cell population selected in this way necessarily contains *inter alia* activated, antigen-specific T lymphocytes. Further selection steps, for example, for the expression of CD4 or CD8 are likewise disclosed.

D2 discloses the detection of CD154-expressing $CD4^+$ T cells in different groups of patients, on the basis of flow cytometry (page 191, column 2, lines 9 to 64). The increased CD40L expression observed in RA patients is ascribed to the increased portion of activated T lymphocytes (page 194, column 1, lines 28 to 31, and column 2, lines 50 to 58).

3. None of the documents mentions or suggests the additional use of CD40/CD154 system inhibitors for purifying or detecting activated T cells.

Therefore claims 1 to 10 meet the requirements of PCT Article 33(2) and (3).

4. Claims 11 to 14 are drafted as "two-step process claims", which attempt to link two different method categories that normally cannot be combined (method of producing a product with the use of this product). In the present case, the production method as described generally in claims 1 to 3 and 4 to 7 does not necessarily result in a novel product; depending on the embodiment (separation parameters, incubation period), it results merely in a partial concentration of activated, antigen-specific T cells or their sub-populations (the claim does not exclude further separation steps). The production method and the use as per claims 1 to 10 thus do not make any technically restrictive contribution to the product itself or its intended uses.

Therefore claims 11 to 14 are unclear (PCT Article 6).

The use of concentrated, activated T cells or sub-populations thereof (CD4+, CD8+), e.g. in cancer therapy or for treating autoimmune diseases, is known from D1 and D4 (D1: page 40, line 14, to page 41, line 21; claims 51, 52, 54; D4: abstract; page 59, line 1, lines 11 to 17).

The claimed uses differ from the prior art as per D1 and D4 only by virtue of features that are irrelevant to the category of claim, i.e. by virtue of the type of T cell selection, but not in terms of the cell population (activated, antigen-specific T cells) used in the therapy.

Therefore, even taking account of the applicant's arguments, claims 11 to 14 are not considered novel (PCT Article 33(2)).

5. The PCT Contracting States have no uniform criteria for assessing the industrial applicability of claims 11 and 12 in their present form. Patentability may also depend on the wording of the claims. The EPO does not, for example, recognize the industrial applicability of claims to the medical use of a compound; it does, however, allow claims to the first medical use of a known compound or to the use of such a compound to manufacture a drug for a new medical application.